Estimating the Risk of Renal Stone Events during Long-Duration Spaceflight

David Reyes, MD, MPH, Eric Kerstman, MD, MPH
Gary Gray, MD, MPH, and James Locke, MD, MPH

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Disclosures

No financial relationships

Off-label use and/or investigational use of drugs or other treatments will not be discussed

Potential Renal Stone Outcomes

- Infection
- Obstruction
- Incapacitation
- Mission failure
- Evacuation
- Long-term disability
- Death

Space Flight Risk Factors

- Fluid shifts in microgravity
- Bone demineralization
- Decreased thirst and fluid intake
- Concentrated urine
- Calcium excretion

Whitson, P. (2001), The risk of renal stone formation during and after long-duration spaceflight, Nephron, 89(3):264-70.

Current ISS Medical Standards

Renal stone is a disqualifying medical condition for long duration space flight

- *Presence or history of urinary calculus*
- Requires a medical waiver

History of Renal Stones in Space Flight

- U.S. Space Program
  - 14 renal stone events among 12 astronauts as of 2008
  - 4 events prior to space flight (no association)
  - 10 events within 2 years postflight
- Russian Space Program
  - 3 renal stone events postflight
  - 1 renal stone event inflight

Inflight Renal Stone Event

- Acute abdominal pain in a cosmonaut on 11/11/82 on Salyut 7 (6 months into a 7 month mission)
- Initially diagnosed as appendicitis
- Caused severe pain and significantly impacted the inflight timeline
- Resolved on-orbit with apparent passing of the stone spontaneously over a period of days
- No medical evacuation
- Mission was completed

Renal Stone Epidemiology

- Lifetime prevalence 10% male, 5% female
- 3.7 % to 4.6% of commercial aviation pilots between 2000 – 2007*
  - Similar to astronaut prevalence

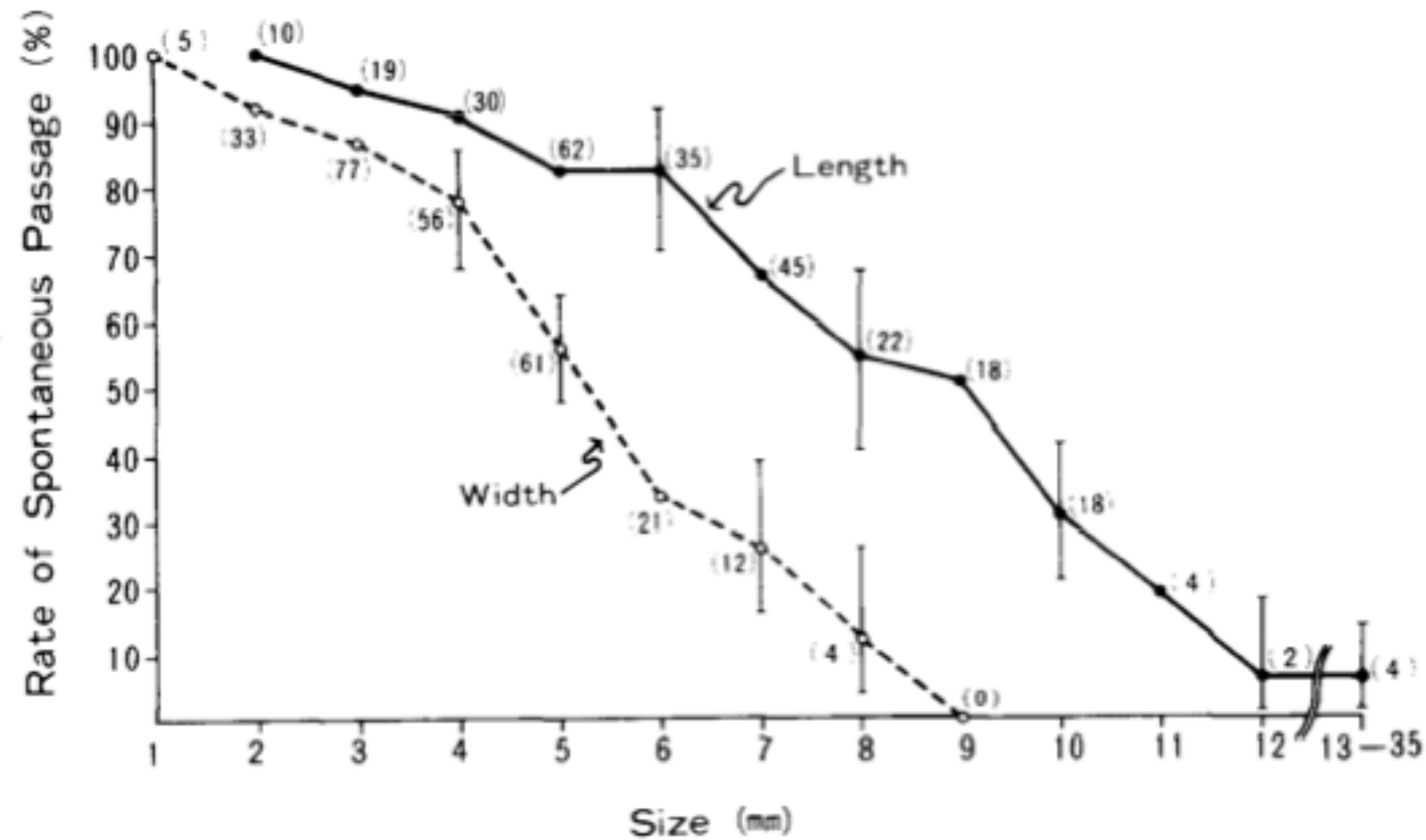
*Hyams, E., et al. (2011) The incidence of urolithiasis among commercial aviation pilots, J Uro, 186:914-916.

Asymptomatic Stones

Size (mm)	Stone Free	Progression	Intervention
< 5	28%	40.4%	5.3%
5 - 10	4.8%	52.4%	9.5%
> 10	0%	71.4%	14.3%

Koh, et al. (2011), *Outcomes of long-term follow-up of patients with conservative management of asymptomatic renal calculi*, BJU Int,109:622-625.

Size vs. Spontaneous Passage



Ueno, et al. (1977) Relation of spontaneous passage of ureteral caliculi to size. J Urol, 10 (6):544-546.

Days to Pass vs. Size

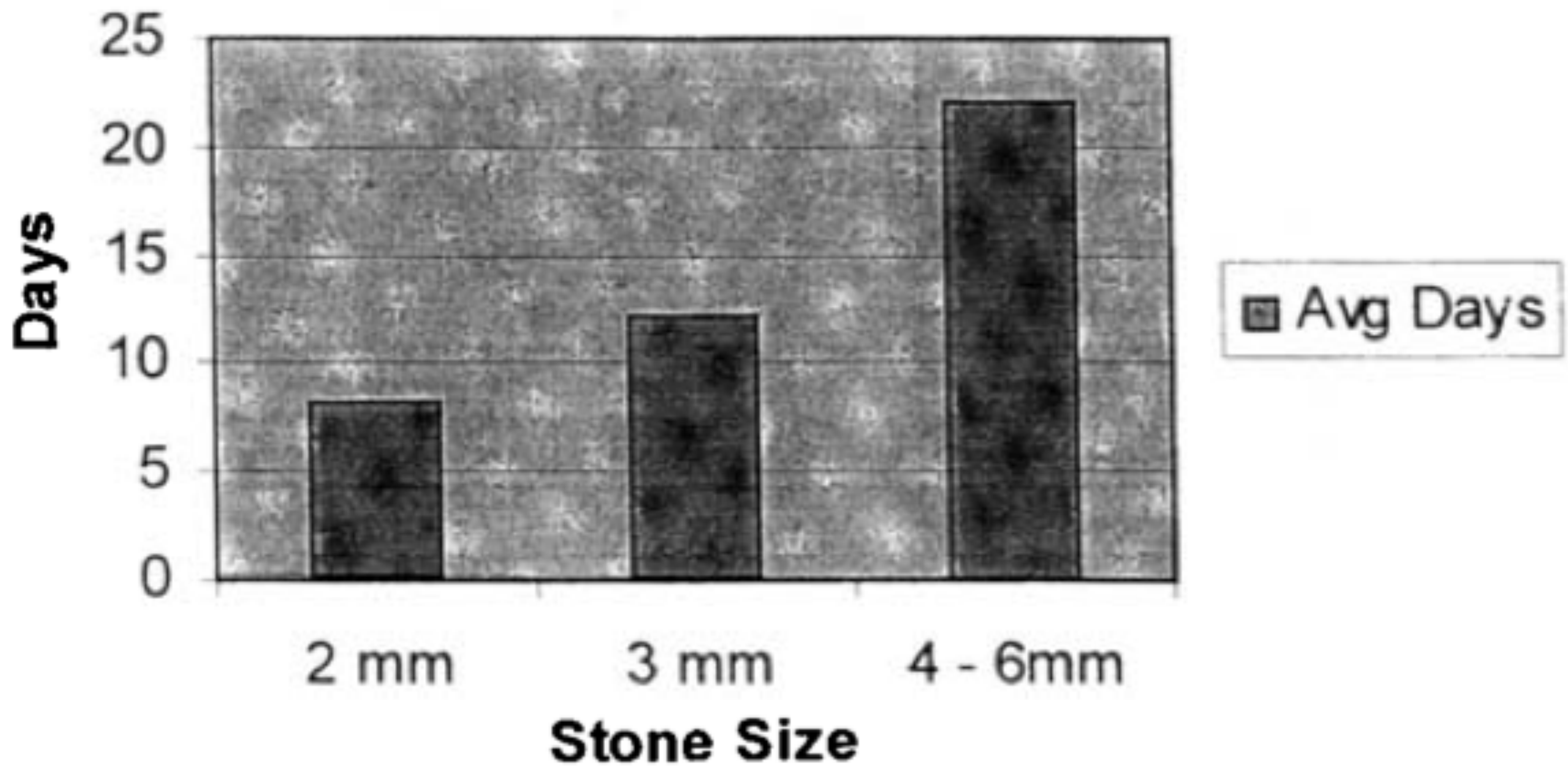


FIG. 1. Average (*avg.*) days to stone passage

Miller, O. & Kane, C. (1999), Time to stone passage for observed ureteral caliculi: A guide for patient education, J Uro, 162:688-691.

Medical Risk Matrix – Long-Duration Missions (ISS) MDC-1

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Renal Stone Risk

	Class 1 Medical Event	Class 2 Medical Event	Class 3 Medical Event	Class 4 Medical Event
	Medical problem with potential long-term health risk to individual but minimal symptoms or signs during mission	Significant medical event, illness, or injury	Major medical illness or injury requiring full medical resource intervention	Acute medical crisis beyond ISS medical resource capabilities
	May cause a moderate reduction in performance	Significant reduction in performance	Major degredation in performance	Loss of critical function
	Can handle with onboard capabilities	Requires extensive medical resource utilization	Full utilization of all available medical resources	Beyond capability of ISS medical resources
	Can handle within designated timeline	May cause failure to meet mission objectives	Planned decrewing (medical evacuation)	Emergency evacuation
Likely ≥2%<5%				
Possible ≥1%<2%				
Unlikely <1%≥0.5%				
Highly unlikely <0.5%				

MSMB Risk-based Decision Analysis

- Low risk – acceptable for MDC 1 disposition (long duration)
- Moderate risk – Further consideration required for an MDC 1 disposition
- High risk – unsuitable for MDC 1 disposition

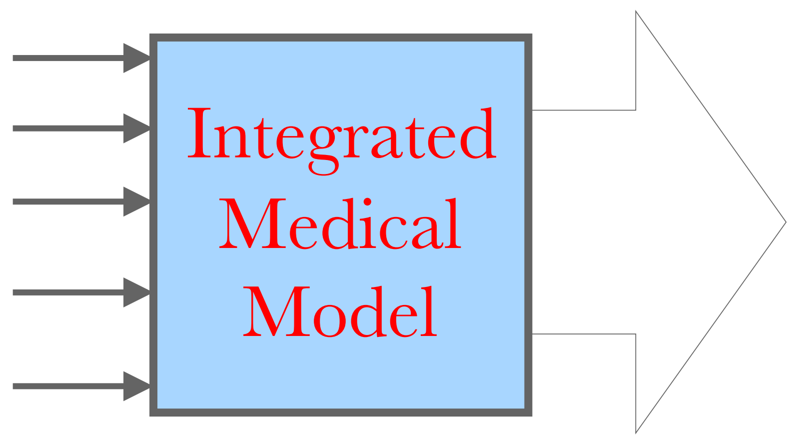
Integrated Medical Model (IMM)

- IMM Background
  - Software model used to simulate human space flight missions
  - Simulates medical events during space flight missions
  - Estimates the impact of these medical events on crew health and mission success
  - Outputs include estimates of crew health, probability of medical evacuation, and probability of medical loss of crew life
  - Optimization routines can be used to design medical systems which maximize crew health and probability of mission success

IMM Conceptual Model

Inputs

- Medical Conditions & Incidence Data
- Crew Profile
- Mission Profile & Constraints
- Potential Crew Impairments
- Potential Mission End States
- In-flight Medical Resources



Outputs

- Medical Condition Occurrences
- Crew Impairments
- Clinical End States
- Mission End States
- Resource Utilization
- Optimized Medical System

Medical Risk Matrix – Long-Duration Missions (ISS)
MDC-1

	Class 1 Medical Event	Class 2 Medical Event	Class 3 Medical Event	Class 4 Medical Event
Astronaut with no history of stones	Medical problem with potential long-term health risk to individual but minimal symptoms or signs during mission	Significant medical event, illness, or injury	Major medical illness or injury requiring full medical resource intervention	Acute medical crisis beyond ISS medical resource capabilities
	May cause a moderate reduction in performance	Significant reduction in performance	Major degredation in performance	Loss of critical function
	Can handle with onboard capabilities	Requires extensive medical resource utilization	Full utilization of all available medical resources	Beyond capability of ISS medical resources
	Can handle within designated timeline	May cause failure to meet mission objectives	Planned decrewing (medical evacuation)	Emergency evacuation
Likely ≥2%<5%				
Possible ≥1%<2%				
Unlikely <1%≥0.5%				
Highly unlikely <0.5%			**Renal Stone (<5mm)**	**Renal Stone (>5mm)**

<u>MSMB Risk-based Decision Analysis</u>

- Low risk – acceptable for MDC 1 disposition (long duration)
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IMM Analysis

Six month ISS mission with 6 crew

- with all crew meeting current med standards

- **Evacuation**

1. Visual Impairment
2. Dental Abscess
3. **Kidney Stone**
4. Sepsis
5. Smoke Inhalation

Three Scenarios

1. No history of stone
2. History of stone
3. Current stone

Hypothetical Case #1

- 38 year old female Astronaut
  - No stone history
  - No findings on imaging
  - Will launch in 2 months to the ISS
  - For a 6 month mission

Risk of developing <u>first</u> stone?

Hypothetical Case #2

- 45 year old male Cosmonaut
  - History of symptomatic 5 mm stone
  - Treated with lithotripsy, resolved
  - Will launch in 2 months to the ISS
  - For a 6 month mission

Risk of developing a <u>new</u> stone?

Hypothetical Case #3

- 42 year old male Astronaut
  - 2 mm calcification in renal parenchyma
  - Asymptomatic
  - Will launch in 2 months to the ISS for a 6 month mission

Risk of becoming <u>symptomatic</u>?

Risk Quantification

- IMM can provide renal stone risk estimates that can be used to assist
  - Crew medical certification decisions
  - Medical resource allocation
  - Crew medical training

Renal Stone Issues

Renal stones are a low likelihood but high consequence event

- What are acceptable waiver criteria?
- Can renal stone events be prevented?
- How do we monitor for stone formation pre-flight and in-flight?
- How do we manage in-flight stones?

Future Work

- Improved risk assessment
- Prevention
- Close monitoring and early detection
- Improved treatments
- Creation of a NASA Renal Stone Clinical Practice Guideline